CARCINOMATOUS METASTASES DEVELOPING OVER THREE YEARS AFTER REMOVAL OF THE BREAST WITHOUT LOCAL RECURRENCE.[1]

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OF fundamental importance in the decision of the question of the curability of cancer by operation is the localized character of the growth. When metastasis has occurred, no matter how thorough the removal of the primary tumor, the continued growth of the secondary deposits will nullify our efforts to obtain a cure. The modern methods enable us to cope with extensive local disease, and to follow it to the nearest lymph nodes with a reasonable hope of thorough eradication, and of freedom from recurrence. But a single distant metastatic deposit renders us practically helpless.

If the presence of a secondary deposit in a situation whence it can be removed by excision of the tumor, or ablation of the affected part or organ, is recognized at the time of proposed removal of the primary tumor, three questions arise: 1st, Shall we remove the primary tumor alone? 2d, Shall we remove both primary and secondary tumors? 3d, Shall we decline any operation?

(1.) In certain cases the primary tumor causes symptoms which seriously inconvenience the patient or threaten life, and then the tumor should be removed if the operation is not too severe, even when the secondary tumor cannot be removed. As there is no hope of a radical cure, extensive operations are not advisable, and, fortunately, comparatively slight operations afford the desired relief in such cases.

(2.) Under certain circumstances, as when the patient is in vigorous condition, when both primary and secondary tumors are easily removable, and when there is absolutely no sign of other deposits of the disease, we might venture on the thorough removal of both tumors. The justification for this course lies in the abundant evidence in careful postmortem examinations that a single secondary tumor may reach a very full development, even sufficient to cause death, without any other metastatic deposits, and that this may occur even while the primary focus is still limited in extent and easy to remove. Such single secondary deposits may develop in the kidney, the other breast, or in a distant bone of the extremities, from a primary carcinoma of the breast, and all of these lesions might offer an opportunity for successful surgical treatment.

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(3) But in my personal experience I cannot recall a case in which the conditions were such as to justify removal of a distant secondary tumor at the time of operation on the primary tumor. Even when the secondary tumor appeared or was discovered after successful removal of the primary focus without local recurrence the conditions have never warranted operation. In every case the patients' general condition has been poor or it seemed probable that other secondary deposits existed although they were not evident. We must conclude, then, that in practice one will rarely meet with a case of malignant disease in which it will be good surgery to remove both the primary lesion and a distant metastasis.

The occurrence of secondary deposits which gave no symptoms and could not be recognized at the time of operation for the original disease, but soon became evident afterwards is unfortunately very common. We need only emphasize the necessity for a careful examination of the entire body before undertaking the removal of a malignant growth, in order to discover, if possible, any such secondary tumors.

Our results in the removal of malignant growths have so greatly improved that we feel fairly confident of freedom from local recurrence if the operation can be performed before the disease has spread too far. This freedom from local recurrence is often spoken of as a cure of the disease and in fact a permanent cure is often effected. But in the individual case we are still uncertain as to the length of time which should elapse without local recurrence before the patient can be considered free from danger of any return. When operations were less complete and thorough than they now are, the number of patients who remained well for three years or more was not very great. It is not surprising, then, that late recurrences locally, or late appearance of secondary tumors, were rarely observed. Now, however, a very large number of persons have survived for long periods after the removal of the primary tumor, and there must be an increasing number of cases with late recurrence. This is indicated by the fact that there is a constant demand for a lengthening of the period which must elapse before a cure can be claimed, even limiting the question to the local or regional recurrences. The old period of three years of freedom from recurrence has been generally discarded and we hear demands for five years, ten years, or even longer periods. If we take into consideration not merely the local recurrences, but include the late-appearing metastases, ten years is not too long, as shown by the following cases operated upon by me. I have reported only those cases in which the secondary deposits were observed three years or more after the removal of the primary tumor, without local recurrence.

CASE I.—Annie C., thirty-seven years of age, married, born in Ireland. Carcinoma of left breast, with slight axillary involvement; removed October 11, 1889, at St. Luke's Hospital. A recurrent nodule formed in the scar and the latter with the entire pectoralis major muscle was removed January 13, 1890. The other breast became carcinomatous and was removed with the pectoralis major December 16, 1892. Dr. H. H. Robinson, of Goshen, examined her and kindly reported November 18, 1895, that there was no sign of recurrence. Soon after vague symptoms of intrathoracic complications arose and she died August 25, 1896, of a secondary tumor in the mediastinum, pushing forward and involving the ribs and sternum on the left side, nearly four years after the last operation. (Letter from Dr. T. D. Mills, of Middletown.)

CASE II.—Florence A. C., thirty-eight years of age, widow, born in United States. Carcinoma of right breast, numerous small glands in axilla. Removed breast and axillary contents March 22, 1894, at the General Memorial Hospital. The wound became slightly infected but healed in about four weeks. She remained well until February, 1904, ten years after the operation, when examination showed some swelling of the sternum and the supraclavicular glands of the opposite (left) side became enlarged. There was no local recurrence. There was dulness on percussion over the sternum and to the left of it, with diminished breathing over most of the left lung. She had a dry cough, resembling the reflex cough of thoracic aneurism. Three weeks later, in a violent fit of coughing she suddenly lost part of the field of vision in the right eye and Dr. E. J. O'Shaugnessy, of New Canaan, wrote that an examination of the eyes revealed a tumor in the fundus. She died in April or May, 1904.

CASE III.—Minerva K., forty-three years of age, married, born in New York. Carcinoma of the left breast; removal with the axillary contents at the General Memorial Hospital, April 11, 1895. She remained well until March 14, 1901, when she complained of dyspnœa and cough and pain in the scar, which remained healthy. Nothing could be found of an abnormal character in the examination of the chest. The symptoms gradually grew worse, and when examined November 30, 1903, marked physical signs of internal thoracic deposit were discovered. There was also great enlargement of the sternum. There was no local recurrence. She has not been seen since, and has probably died.

CASE IV.—Mary A. B., sixty-five years of age, married, born in New York. Carcinoma of the left breast, several nodules following a chronic mastitis. Breast and axillary contents removed at the General Memorial Hospital March 21, 1896. I saw her October 18, 1899. She had hematuria and the left kidney was enlarged. The scar was healthy. March 8, 1901, Dr. G. A. Crump wrote that she still had hematuria, and that there was a growth in the vagina which felt like colloid material and bled readily. The breast scar remained free from recurrence. She died soon afterwards.

CASE V.—Harriet E. K., forty-nine years of age, married born in New Jersey. Carcinoma of the right breast, glands small but extensively involved. Breast and axillary contents removed at the General Memorial Hospital, April 27, 1896. In August, 1899, I examined her and found no local recurrence. She had some vague nerve symptoms which I ascribed to hysteria and morphine addiction, as both conditions were present. Soon after, paralysis slowly developed, with curvature of the spine and severe neuralgic pains. She died in March, 1901, and Dr. J. Arthur Booth, who had charge of her towards the end and made the autopsy, kindly informed me that he found carcinoma of the vertebræ and some nodules also in the spleen.

I could add to these some cases of tumors in other situations, such as a pylorectomy for carcinoma remaining well until a tumor of the iliac bone developed five years later; and a sarcoma of the foot treated by local excision, without local return, but the patient died of pulmonary sarcoma in three years. But in order to make the material homogeneous I have limited the cases to those associated with tumor of the breast.

I have made no search in the literature for similar cases, as I believe that the cases there are as yet too isolated to be of much value, but the following were at hand and may be mentioned:

Poulsen (*Arch. f. kl. Chir.* xlii. S. 616,) reported three cases of amputation of the breast with late metastases, the patients dying from five to eight years after the operation. Schmidt (*Deuts. Zeitschr. f. Chir.* xxvi. S. 139), recorded a case of death from metastasis in lungs and liver seven years after removal of the breast. Clairmont (*Arch. f. kl. Chir,* 1904, lxxiii. S. 620) reported a case of late metastasis in the bronchial glands ten years after a nephrectomy for adrenal tumor. König (*Verh. Deutsche chirurg. Congress,* 1903, S. 72) mentioned two cases of late secondary in the neck, ten and thirteen years after removal of the breast. Lomer (*Zeitschr. f. Geb. & Gyn.* Bd. 50, S. 358) quoted from Lubarsch (personal communication) an autopsy on a woman who died of pneumonia, whose left breast had been amputated five years before, microscopic examination of the axillary glands on the left side showing carcinomatous nodules present in them, but the cells showed no mitoses. Petersen (*Beitr. z. kl. Chir.* 1904, xliii. S. 171) quoted a case of von Beck in which a patient died of intestinal obstruction three years after a pylorectomy, and a small carcinoma was found in the sigmoid flexure and also a nodule of carcinoma in the center of a small uterine fibroid.

There had been no recurrence in the stomach. Labhardt (*Beitr. z. kl. Chir,* xxxiii. S. 571) collected several cases, of which two can be added to our list, death from metastasis in the liver five years after removal of breast (von Meyer); and in the lung ten years after a similar operation (Jones and Platt).*

Two hypotheses suggest themselves by which to explain these peculiar cases. We may suppose that these late-developing tumors are independent growths, an hypothesis which will account for some cases very readily, especially when the secondary tumor lies in an organ commonly attacked by primary carcinoma, such cases as involvement of the other breast after one has been removed, or of cancer of the stomach or uterus following cancer of the breast. But the numerous cases with involvement of lungs and liver, organs in which primary carcinoma is rare, do not admit of this explanation. Secondly, we may suppose that the cells from which the secondary tumors spring may have been deposited before the removal of the primary tumor, but have lain latent or developed so slowly that they do not become clinically evident for many years. Opposed as this theory is to our preconceived ideas of the growth of carcinoma, and especially of the tumors secondary to carcinoma of the breast, there is considerable pathological evidence of its probability. When a late local recurrence also takes place we have clear proof that some cells left by the operation have lain latent, and these are not so uncommon, but in our cases there was no local return.

Such authorities as W. Petersen (*loc. cit.*), Lubarsch (*Zur Lehre v. d. Geschwülsten u. Infektionskrankheiten*), M. B. Schmidt (*Die Verbreitungswege der Karzinome u. s. w.,* Fischer, Jena, 1903), Lomer (*loc. cit.*), Fraenkel (*Wien. kl. Wch.* 1898, S. 465) and Schuchardt (*Centr. f. Gynek.* 1901, S. 664) argue that in most cases of carcinoma the actual metastases are much more frequent than supposed, and that probably few primary operations really eradicate all the disease, yet an apparent cure may be obtained lasting for many years. The carcinomatous deposits left behind remain latent

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*See also Schroeder, *Beitr, z. kl. Chir.* xlv. S. 685-6, Fälle 6, 7, 9, 10, 12, 13.

and may even undergo retrogressive changes as in Schuchardt's case, in which peritoneal nodules with ascites were found when a carcinoma of the pylorus was removed, yet on autopsy after death from pleurisy over two years later, not only was there no recurrence in the stomach, but the peritoneal nodules had entirely disappeared. We know well how the tissues and cells resist various bacterial infections by phagocytosis, by encapsulation with fibrous tissue, or by direct action of antitoxines upon the bacteria. It is not impossible to imagine that the carcinoma cells could be attacked by the same means, and we can even form the hypothesis that a thorough removal of the primary tumor may not only get rid of the local disease, but may have a beneficial effect upon the resistance of the tissues to the secondary deposits. So much is now appearing with regard to cytolytic ferments and their actions that it seems quite within the bounds of probability to suppose that the large mass of cells in the primary tumor may keep in circulation some chemical bodies which unfavorably affect the resistance of the tissues, and that the removal of this factory of toxic substances might restore the normal resisting power, and enable the tissues to destroy or encapsulate small deposits of cancer cells.

It might be well to note the bearing of these facts and theories upon the usefulness of the operative treatment of cancer. While the cases related detract somewhat from the brightness of the prospects for a radical cure by operation, the number of persons who suffer from these late appearing metastases is not large in comparison with the number of persons who remain free from local recurrences after successful removal of tumors. Even in these cases the interval of freedom is in itself enough to prove the practical usefulness of the primary operation, especially if it approximate ten years. A free interval of ten years at the time of life when the majority of the operations for cancer are performed affords a practical cure, for many of the patients will die of other causes before the disease returns or develops. It cannot be argued that if we cannot remove the disease entirely there is no use in the operation, neither can it be said that operations should be less extensive, leaving the remainder to be dealt with by the resistance of the tissues. Practical experience is against both of these assertions, for the results have improved with the enlargement of the scope of operation. We may even claim that the facts are encouraging, because formerly we had supposed that immediate and prompt recurrence was to be expected when we left behind even the smallest portions of disease, whereas in the light of this evidence we can hope that minute cancerous deposits can be checked in growth or annihilated. Further, if our theory is correct, the removal of the primary tumor assists in this result. Similar effects are seen in the operations for removal of foci of tuberculous disease, for here, too, the results improve with the extension of the operations, and it is well known that the individual is assisted in his combat against a more or less general infection by being relieved of the principal mass of infected tissues.